Rational Design of Pharmaceutical and Other Liquid Formulations

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Every year pharmaceutical, health-care and related industries invest a high percentage of their total time and resources on development of new products and improvement of existing (pharmaceutical) formulations. Product development is still mainly based on trial and error experimentation and laboratory procedures, indicating long research processes without any certainty of a definitive solution and far from achieving the *optimal formulation* of the product. Besides, (pharmaceutical) ingredients to be used for the experimentations are often very expensive and not available in the desired form or at the desired level of purity. Moreover, the experimental procedures are affected by unavoidable errors due to the complicated and often not-standardized procedures. Therefore, the need for a rational and systematic model-based approach to plan suitable experimental designs would constitute a fairly useful tool for pharmaceutical product design and product design in general. A model-based approach significantly reduces the number of experiments necessary for product design and at the same time gives a clear idea about the direction to take for further (reduced) experimentation. In such a way tedious and uncertain screening processes can be avoided with sensible reduction of both time and resources for the product launch on the market.

Identification of a pure solvent or anti-solvent for a specific Active (Pharmaceutical) Ingredient (API or AI) is a problem of major concern for the pharmaceutical and related R&D departments. Solvents, lipids and other compounds are commonly employed in product formulations as well as in API processing. In addition, the screening of several solvent mixtures that sometimes show improved characteristics of solubility toward a particular API is necessary. Besides, in liquid formulated products, API (or AI) needs to be mixed with additives to enhance the product quality and solvents to deliver the product.

This work presents a model-based method for solvent screening and solvent mixture design for pharmaceutical applications and API/AI based liquid formulated products. Two cases are investigated: a case where the solvent or solvent blend is designed for API processing (here the solvent is not part of the final API based product), and a case where the solvent or solvent blend is part of the API/AI based formulated product. In both cases, the solubility of the API/AI needs to be predicted in solvents (single solvent or blends). A general solubility modelling procedure having different options for the solubility calculation (such as UNIFAC, UNI-sac and PC-SAFT) is employed. A unique feature of this solubility calculation procedure is that it is truly predictive and does not need any new experimental data for the computer-aided design stage of the formulation design methodology (Conte *et al*. 2011).Once the domain search has been reduced to a few solvents or solvent mixtures, solubility can be computed by correlative models such as NRTL-SAC andPC-SAFT.

The newly developed method described above is to be integrated in a comprehensive framework for formulation design that was previously developed and tested for personal care products. Such a method was implemented in the software ‘the virtual product-process design laboratory’ (vPPD-lab) (Conte *et al.*, 2011).

Examples illustrating the application of the procedure for solvent, solvent-blend and/or AI-based formulation design will be presented. Also, a conceptual case study validating the models and the design steps involving the design of a solvent mixture that maximizes the API solubility as well as the identification of an optimal anti-solvent for a well-known API such as paracetamol will be presented.

References

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